

DOCKET NO.: 3DP-0456
Application No.: 09/826,210
Office Action Dated: June 2, 2003

PATENT

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1-38 (Cancelled).

39. (Previously presented) A method of stimulating cell division which comprises:

(A) contacting cells with an effective amount of one or more muteins of a human basic fibroblast growth factor, or biologically active peptides thereof *in vitro*, wherein said one or more muteins comprise the substitution of a neutral and/or hydrophobic amino acid for one or more of the following:

- (a) Glutamate 89; or
- (b) Aspartate 101; or
- (c) Leucine 137;

wherein the numbering of amino acids is based on SEQ ID NO: 1; or

(B) contacting cells with an effective amount of said one or more muteins, or biologically active peptides thereof *in vivo*.

40-53 (Cancelled).

48. (Currently amended) The method of ~~any one of~~ claims 39, 41 ~~or~~ 42, wherein said one or more muteins comprise the substitution of a hydrophobic amino acid for Glu⁸⁹.

49. (Currently amended) The method of ~~any one of~~ claims 39, 41 ~~or~~ 42, wherein said one or more muteins comprise the substitution of a hydrophobic amino acid for Asp¹⁰¹.

50. (Currently amended) The method of ~~any one of~~ claims 39, 41 ~~or~~ 42, wherein said one or more muteins comprise the substitution of a hydrophobic amino acid for Leu¹³⁷.

51. (Currently amended) The method of ~~any one of~~ claims 39, 41 ~~or~~ 42, wherein said one or more muteins comprise the substitution of a neutral amino acid for Glu⁸⁹.

52. (Currently amended) The method of ~~any one of~~ claims 39, 41 ~~or~~ 42, wherein said one or more muteins comprise the substitution of a neutral amino acid for Asp¹⁰¹.

DOCKET NO.: 3DP-0456
Application No.: 09/826,210
Office Action Dated: June 2, 2003

PATENT

53. (Currently amended) The method of ~~any one of~~ claims 39, 41 ~~or~~ 42, wherein said one or more muteins comprise the substitution of a neutral amino acid for Leu¹³⁷.

54. (Currently amended) The method of ~~any one of~~ claims 39, 41 ~~or~~ 42, wherein said neutral amino acid is defined as alanine and said hydrophobic amino acid is defined as tyrosine.

55. (Currently amended) The method of ~~any one of~~ claims 39, 41 ~~or~~ 42, wherein said one or more muteins of human basic fibroblast growth factor, or biologically active peptides thereof, comprise one or more of the following substitutions:

- (a) substitution of Glutamate 89 with alanine or tyrosine;
- (b) substitution of Aspartate 101 with alanine; or
- (c) substitution of Leucine 137 with alanine;

or any combination thereof, wherein the numbering of amino acids is based on SEQ ID NO:1.

62. (Previously presented) The method of claim 61, wherein said mutein is human basic fibroblast growth factor [Ala⁸⁹].

63. (Previously presented) The method of claim 61, wherein said mutein is human basic fibroblast growth factor [Ala¹⁰¹].

64. (Previously presented) The method of claim 61, wherein said mutein is human basic fibroblast growth factor [Ala¹³⁷].

65. (Previously presented) The method of claim 61, wherein said mutein is human basic fibroblast growth factor [Ala^{89, 101}].

66. (Previously presented) The method of claim 61, wherein said mutein is human basic fibroblast growth factor [Ala^{89, 137}].

67. (Previously presented) The method of claim 61, wherein said mutein is human basic fibroblast growth factor [Ala^{101, 137}].

68. (Previously presented) The method of claim 61, wherein said mutein is human

DOCKET NO.: 3DP-0456
Application No.: 09/826,210
Office Action Dated: June 2, 2003

PATENT

basic fibroblast growth factor [Ala^{89, 101, 137}].

69. (Previously presented) The method of claim 61, wherein said mutein is human basic fibroblast growth factor [Tyr⁸⁹].

70. (Currently amended) The method of ~~any one of~~ claims 39, 41 ~~or~~ 42, wherein said mutein is a human basic fibroblast growth factor [Tyr¹³⁷].

71. (Currently amended) The method of ~~any one of~~ claims 39, 41 ~~or~~ 42, wherein said mutein is a human basic fibroblast growth factor [Tyr^{89, 101}].

72. (Currently amended) The method of ~~any one of~~ claims 39, 41 ~~or~~ 42, wherein said mutein is a human basic fibroblast growth factor [Tyr^{89, 137}].

73. (Currently amended) The method of ~~any one of~~ claims 39, 41 ~~or~~ 42, wherein said mutein is a human basic fibroblast growth factor [Tyr^{101, 137}].

74. (Currently amended) The method of ~~any one of~~ claims 39, 41 ~~or~~ 42, wherein said mutein is a human basic fibroblast growth factor [Tyr^{89, 101, 137}].

75. (Previously presented) The method of claim 39, wherein said method comprises contacting cells *in vivo*.

76. (Previously presented) The method of claim 39, wherein said effective amount *in vitro* is 0.001 picograms to 1000 micrograms per milliliter.

77. (Previously presented) The method of claim 76, wherein said effective amount is 0.001 nanograms to 1000 nanograms per milliliter.

78. (Previously presented) The method of claim 77, wherein said effective amount is 0.01 nanograms to 100 nanograms per milliliter.

79. (Previously presented) The method of claim 39, wherein said effective amount *in vivo* is from about 0.001 pg/kg body weight to about 10 mg/kg body weight daily administered parenterally.

80. (Previously presented) The method of claim 79, wherein said effective amount is from about 1 pg/kg body weight to 5 mg/kg body weight per day.

DOCKET NO.: 3DP-0456
Application No.: 09/826,210
Office Action Dated: June 2, 2003

PATENT

81. (Previously presented) The method of claim 80, wherein said effective amount is from about 10 pg/kg body weight to about 1 mg/kg body weight daily.

82-83 (Cancelled).

84. (Currently amended) The method of ~~any one of~~ claims 39, 41, ~~or~~ 42, wherein said neutral amino acid is selected from the group consisting of serine, threonine, alanine, asparagine, glutamine, cysteine, and glycine, and said hydrophobic amino acid is selected from the group consisting of tyrosine, leucine, isoleucine, valine, proline, phenylalanine, tryptophan, and methionine.